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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,371	06/13/2001	Zhong-Min Wei	21829/91 (EBC-007)	4973

7590 11/07/2002

Michael L. Goldman
NIXON PEABODY LLP
Clinton Square
P.O. Box 31051
Rochester, NY 14603

EXAMINER	
KUBELIK, ANNE R	
ART UNIT	**PAPER NUMBER**
1638	15

DATE MAILED: 11/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/880,371	Applicant(s) WEI ET AL.	
	Examiner Anne R. Kubelik	Art Unit 1638	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *22-74* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-21) and *Erwinia* hypersensitive response elicitors in Paper No. 12 is acknowledged. The traversal is on the ground(s) that searching Groups I and II would require common areas of search and consideration. Applicant also urges that restriction among elicitors from different pathogens, other than *Phytophthora*, is improper. Applicant urges that many of the claims of Group I are generic to the type of elicitor and thus restriction to an individual one is unwarranted. Furthermore, Applicant urges that Bonas (I), Bonas (II) and Preston et al teach that hypersensitive response elicitor proteins fall within a recognized class of proteins and are defined by particular characteristics. Applicant urges that claim 1 is a generic linking claim and should be treated accordingly. Applicant urges that the restriction between Groups I and II should be withdrawn.

This is not found persuasive. The methods of groups I and II require different starting materials, have different method steps and produce different products and thus do not require common areas of search and consideration.

Bonas (II) teaches that the sequence identity between hrp proteins varies is as low as 29%, and not all are functionally homologous (pg 85, paragraph 1-2). Additionally, Applicant points out in the response that hypersensitive response elicitors from fungi like *Phytophthora* are quite different from those from bacteria. Thus, there is no structural feature that characterizes these proteins.

A search on Group I and *Erwinia* hypersensitive response elicitors found art on other hypersensitive response elicitors, and as a courtesy to Applicant, claims 1-21 will be examined in their entirety.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 22-74 are withdrawn from consideration as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of topical application of any of a multitude of hypersensitive response elicitor proteins from any source to plants transformed with any of a multitude of DNA molecules that impart a transgenic trait to a plant, particularly ones that are associated with a deleterious effect.

In contrast, the specification only describes the hypersensitive response elicitor protein, $harpin_{Ea}$ and corn plants of cultivar "Rogers", which is Bt transformed. Applicant does not describe the other hypersensitive response elicitor proteins and plants comprising other transgenic traits that are associated with a deleterious effect encompassed by the claims, and the structural features that distinguish all such proteins and nucleic acids from other proteins and nucleic acids are not provided.

Because the proteins and plants are not described, the method of using the proteins and plants is likewise not described, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the compositions used in the claimed methods, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

5. Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of topical application of $harpin_{Ea}$ to transformed and non-transformed plants, does not reasonably provide enablement for a method of topical application

of hypersensitive response elicitor proteins to plants comprising any transgenic trait that is associated with any deleterious effect. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a method of topical application of any of a multitude of hypersensitive response elicitor proteins from any source to plants transformed with any of a multitude of DNA molecules that impart a transgenic trait to a plant, particularly ones that are associated with a deleterious effect.

The instant specification, however, only provides guidance for application of a 3% solution of $harpin_{Ea}$ (SEQ ID NO:3) on cotton varieties that were transformed with genes encoding Bt toxin and one or more other traits to produce plants that had greater yields (number of bolls) than untreated plants (examples 1-3); this increased yield occurred even when nematode-sensitive plants were grown in nematode infested fields and sprayed with $harpin_{Ea}$ (example 4). The instant specification also provides guidance for application of the $harpin_{Ea}$ solution to Bt and non-Bt transformed corn to produce plants that in both cases had increased resistance to fall armyworm (example 5). The instant specification also provides very general guidance for producing herbicide, insect and pathogen resistant plants, and plants with enhanced nutrient value (examples 6-8 and 10). The instant specification also provides a very general discussion of transgenic traits, like glyphosate resistance and Bt-conferred resistance, that while providing some advantages to the plant also produce disadvantages, like decreased yield or susceptibility to other diseases (example 9).

The instant specification fails to provide guidance for other hypersensitive response elicitor proteins or for plants comprising other transgenic traits that are associated with a deleterious effect. The specification does not teach which hypersensitive response elicitor proteins compensate for the deleterious trait of which transgenic trait.

Not all deleterious effects associated with transgenic traits can be overcome by the topical application of a hypersensitive response elicitor protein. Dong et al (1999, Plant J. 20:207-215) teach the topical application of harpin on *Arabidopsis* plants transformed with the transgenic trait NahG, which renders the plants SAR-compromised; harpin did not overcome the SAR defect nor did it induce resistance to the pathogens *Peronospora parasitica* or *Pseudomonas syringae* pv tomato DC3000(pg 209, left column, paragraph 1, and paragraph spanning the columns on pg 210).

As the specification does not describe the transformation of any plant with a gene that imparts a transgenic trait that is associated with a deleterious effect, undue trial and error experimentation would be required to screen through the myriad of hypersensitive response elicitor proteins and the myriad of transgenic traits encompassed by the claims and plants transformed therewith, to identify those that can be used in the instantly claimed method, *i.e.*, those in which a hypersensitive response elicitor protein overcomes the deleterious effect, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections.

Claim 1 is indefinite because the preamble of the method is missing an indication of what the method is for (*i.e.* a method of imparting disease resistance to plant).

Claims 4 and 14 are indefinite in their recitation of "applying is carried out by ... leaf abrasion at a time proximate to when said applying takes place." Leaf abrasion itself, without the additional step of spraying, injecting or dusting the protein on the leaf, is not a method of applying.

Claim 12 lacks antecedent basis for the limitation "the transgenic plant" in line 3.

Claim 12 is indefinite in its recitation of "the transgenic trait is associated with a deleterious effect ... in the transgenic plant". It is not clear what it means for a trait to be associated with a deleterious effect. Also, what is the trait deleterious relative to?

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Qiu et al (WO 98/24297).

Qiu et al teach a method of imparting disease resistance to a transgenic plant or seed comprising the steps of providing a plant or seed comprising a transgene encoding a hypersensitive response elicitor and applying, by spraying, injection, dusting or immersion, the hypersensitive response elicitor protein of their invention, alone or in a composition comprising a carrier like water, an aqueous solution, a slurry or a powder wherein the composition contains greater than 500 nM of the protein, to the plant or seed (paragraph spanning pg 36-37; claim 53; pg 35, paragraph 3).

10. Claims 1-10 rejected under 35 U.S.C. 102(b) as being anticipated by Bogdanove et al (WO 99/07206).

Bogdanove et al teach a method of imparting disease resistance to a transgenic plant or seed comprising the steps of providing a plant or seed comprising a transgene encoding a hypersensitive response elicitor and applying, by spraying, injection, dusting or immersion, a hypersensitive response elicitor protein, alone or in a composition comprising a carrier like water, an aqueous solution, a slurry or a powder wherein the composition contains greater than 500 nM of the protein, to the plant or seed (pg 30, paragraph 2, and paragraph spanning pg 26-27).

11. Claims 1-14, 17-18 and 20-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Keller et al (1999, Plant Cell 11:223-235).

Keller et al teach plants transformed with a transgene that comprises the coding sequence for cryptogein operably linked to a plant defense promoter (paragraph spanning the columns on

pg 225). Keller et al teach a method of applying *Phytophthora parasitica* var *nicotianae*, which comprises the hypersensitive response elicitor protein cryptogein (pg 225, right column, paragraph 2) to these plants. Application was by leaf abrasion, stem injection or topical application (paragraph spanning the columns on pg 227). The transgenic trait on the transgene is associated with a deleterious effect on disease resistance because these plants were not resistant to *Erysiphe cichoracearum* (pg 228, right column, paragraph 1) and would inherently confer some other deleterious effect under at least one condition. The method of applying *P. parasitica* var *nicotianae* to these plants would inherently enhance their disease resistance. In *P. parasitica* var *nicotianae* the hypersensitive response elicitor protein is inherently in an aqueous carrier. Keller et al also teach a method of applying the isolated protein $Harpin_{Pss}$, a hypersensitive response elicitor from *Pseudomonas syringae* pv *syringae*, by infiltration of the leaves of these plants (pg 230, right column, paragraph 2). This application would inherently enhance disease resistance in these plants and thereby would inherently overcome the deleterious effect.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over each of Qiu et al and Bogdanove et al.

The claims are drawn to a method of imparting disease resistance to a transgenic plant or seed comprising the steps of providing a plant or seed comprising a transgene and applying a hypersensitive response elicitor protein to the plant or seed. The claims are also drawn to such a method where the transgene imparts a transgenic trait that is associated with a deleterious effect on growth, stress tolerance, disease resistance or insect resistance, and wherein applying the hypersensitive response elicitor protein overcomes the deleterious effect.

In addition to the teachings discussed above, Qiu et al teach the topical application of an isolated hypersensitive response elicitor protein from *Erwinia amylovora* on non-transgenic tomato seeds or plants (examples 1 and 8) and the topical application of hypersensitive response elicitor proteins from *Pseudomonas syringae*, *P. solanacearum*, *Xanthomonas campestris*, or *Phytophthora* to seeds or plants (claims 1-24). Qiu et al do not disclose the topical application those specific proteins on transgenic seeds or plants.

In addition to the teachings discussed above, Bogdanove et al teach a method of imparting disease or insect resistance to a plant or enhancing growth in a plant by the topical application of an isolated hypersensitive response elicitor protein from *Erwinia amylovora* on seeds or plants (claims 20-28). Bogdanove et al do not disclose the topical application this proteins on transgenic seeds or plants.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of topical application of an isolated hypersensitive response elicitor protein from *Erwinia amylovora* on seeds or plants, as taught by each of Qiu et al and Bogdanove et al, to apply that protein to transgenic plants or seeds, including those in which the transgenic trait is associated with a deleterious effect. One of ordinary skill in the art would have

been motivated to do so because so many common crop plants have transgenic traits like glyphosate resistance and Bt-conferred resistance; topical application of a hypersensitive response elicitor protein, like the topical application of other pesticides, would be a common technique for use on these plants when they are grown in the field, as plants are commonly sprayed with pesticides. Some of these transgenic traits would be associated with a deleterious effect, like decreased yield or susceptibility to other diseases. Additionally, because Qiu et al claim that hypersensitive response elicitor proteins from *E. chrysanthemi*, *E. amylovora*, *P. syringae*, *P. solanacearrum*, *X. campestris* pv *glycines* and *X. campestris* pv *pelargonii* are their invention (pg 16-26), it would be obvious to use these particular hypersensitive response elicitor proteins in the method of method of imparting disease resistance to a transgenic plant or seed.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
October 28, 2002

Amy Nelson

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600